Gastric non-*Helicobacter pylori Helicobacter* infections: origin and significance for human health

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Besides the well-known gastric pathogen *Helicobacter pylori*, other helicobacters with typical spiral morphology have been detected in a minority of human patients presenting for upper gastrointestinal endoscopy. This group of non-*H. pylori* helicobacters (NHPH), also referred to as *H. heilmannii* sensu lato, includes gastric *Helicobacter* species colonizing the stomach of carnivores and *H. suis*, naturally colonizing the stomach of pigs. Previous epidemiological reports have suggested that direct contact with animals, especially pigs, is a risk factor for humans to contract an infection with one of these bacteria. Recently, we also demonstrated the presence of viable *H. suis* bacteria in pork samples, suggesting that pork can serve as a source of *H. suis* infections for humans. Disregarding the source of infection, NHPH can cause severe gastric pathology in rodent models of human gastric disease. In contrast to the predominant Th1/Th17 inflammatory response associated with a *H. pylori* infection, *H. suis* rather causes a Th2/Th17 response, which may lead to the development of MALT lymphoma-like lesions, indeed observed in long-term infected Mongolian gerbils. Besides a pronounced inflammatory response, *H. suis* also causes necrosis of parietal cells in experimentally infected mice and gerbils, despite the absence of homologues of known *H. pylori* virulence factors such as the *cag*PAI and VacA. Recently, we have identified *H. suis* GGT as the key cell death-inducing factor. Through degradation of reduced glutathione into its degradation products, *H. suis* (and *H. pylori*) GGT causes an increase of extracellular H_2O_2 concentrations, generated in a cell-independent manner and causing lipid peroxidation. This leads to different types of cell death, including apoptosis and necrosis/oncosis, depending on the amount of extracellular glutathione available as a GGT substrate. In conclusion, our findings clearly show that, in humans suffering from gastric disease, the possible involvement of NHPH, including *H. suis*, should not be neglected.